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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

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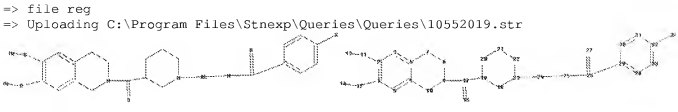

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11  12  13  14  16  17  24  25  26  27  34
ring nodes :
1  2  3  4  5  6  7  8  9  10  18  19  20  21  22  23  28  29  30  31  32  33
chain bonds :
1-12  2-11  9-17  11-13  12-14  16-17  17-19  23-24  24-25  25-26  26-29  26-27
32-34
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  18-19  18-23  19-20  20-21
21-22  22-23  28-29  28-33  29-30  30-31  31-32  32-33
exact/norm bonds :
1-12  2-11  4-7  5-10  7-8  8-9  9-10  9-17  16-17  18-19  18-23  19-20  20-21  21-
22  22-23  23-24  24-25  25-26  26-27
exact bonds :
11-13  12-14  17-19  26-29  32-34
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  28-29  28-33  29-30  30-31  31-32  32-33
isolated ring systems :
containing 1 : 18 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  16:CLASS  17:CLASS  18:Atom  19:Atom
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L4             4 L3

=> s l4 and pd< april 2003
      23709234 PD< APRIL 2003
                 (PD<20030400)
L5             1 L4 AND PD< APRIL 2003

=> dis l5 fbib abs hitstr

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2000:881143  CAPLUS  Full-text
DN   134:42075
```

TI Preparation of novel isoquinoline derivatives as If current inhibitors
IN Watanabe, Toshihiro; Kakefuda, Akio; Okazaki, Toshio; Masuda, Noriyuki; Wada, Koichi
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000075133	A1	20001214	WO 2000-JP3564	20000601	<--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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				WO 2000-JP3564	W 20000601	
	EP 1186601	A1	20020313	EP 2000-931652	20000601	<--
	EP 1186601	B1	20040324			
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	CN 1136213	B	20040128	CN 2000-808270	20000601	
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	AT 262518	T	20040415	AT 2000-931652	20000601	
				JP 1999-156217	A 19990603	
				WO 2000-JP3564	W 20000601	
	PT 1186601	T	20040630	PT 2000-931652	20000601	
				JP 1999-156217	A 19990603	
	ES 2214276	T3	20040916	ES 2000-931652	20000601	
				JP 1999-156217	A 19990603	
	JP 3741042	B2	20060201	JP 2001-502416	20000601	
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				WO 2000-JP3564	W 20000601	
	US 6573279	B1	20030603	US 2001-980402	20011203	
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OS MARPAT 134:42075
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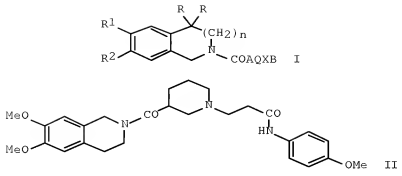

AB Title compds. [I; R = H, CH3; R1 = H, OCH3; R2 = H, OCH3; n = 1, 2; Q = CH2, CH2CH2, CH2CH2CH2; X = CONH, NHCO; A = pyrrolyl, pyrrolidinyl, piperidinyl; B = benzene, indenyl, pyridinyl, benzofuryl, etc.], stereoisomers, and salts having If current inhibitory effect without serious side effects such as convulsion are prepared and drugs, particularly cardiac rate lowering agents containing title compds. as active ingredient are discussed. Title compds. are useful in preventing ischemic heart diseases such as precordial anxiety (thoracic precordial anxiety) and myocardial infarct, and circulatory diseases such as congestive heart failure and arrhythmia (supraventricular arrhythmia, etc.). Thus, the title compound II was prepared

IT 312752-77-5P 312752-79-7P 312752-81-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinoline derivs. as If current inhibitors)

RN 312752-77-5 CAPLUS

CN Benzamide, N-[2-[3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-2,4-difluoro-, ethanedioate (1:1) (CA INDEX NAME)

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CRN 312752-76-4
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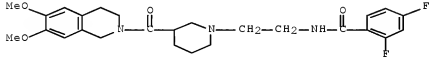


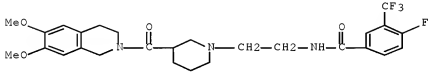
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 312752-79-7 CAPLUS
CN Benzamide, N-[2-[3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-3-(trifluoromethyl)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 312752-78-6
CMF C27 H31 F4 N3 O4



CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 312752-81-1 CAPLUS
CN Benzamide, 3-chloro-N-[2-[3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-, ethanedioate (1:1) (CA INDEX NAME)

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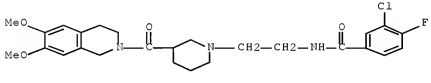
CRN 312752-80-0
CMF C26 H31 Cl F N3 O4



CM 2

CRN 144-62-7
CMF C2 H2 O4

IT 312752-51-5P 312752-71-9P 312752-86-6P
312752-88-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinoline derivs. as If current inhibitors)

RN 312752-51-5 CAPLUS

CN Benzamide, N-[2-[3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-3,4-difluoro-, ethanedioate (1:1) (CA INDEX NAME)

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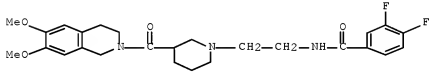
CRN 312752-50-4
CMF C26 H31 F2 N3 O4



CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 312752-71-9 CAPLUS

CN Benzamide, N-[2-[3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-, ethanedioate (1:1) (CA INDEX NAME)

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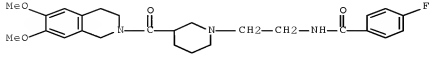


CM 2

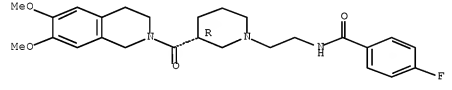
CRN 144-62-7
CMF C2 H2 O4

RN 312752-86-6 CAPLUS
CN Benzamide, N-[2-[(3R)-3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 312752-85-5
CMF C26 H32 F N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

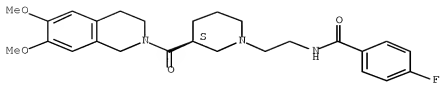
CRN 7664-38-2
CMF H3 O4 P

RN 312752-88-8 CAPLUS
CN Benzamide, N-[2-[(3S)-3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 312752-87-7
CMF C26 H32 F N3 O4

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l4 not l5
L6 3 L4 NOT L5

=> dis l6 1-3 bib abs fhitstr

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:220250 CAPLUS Full-text
DN 146:221125
TI Therapeutic agent for atrial fibrillation
IN Wada, Koichi; Masuda, Noriyuki; Taniguchi, Keiichi
PA Astellas Pharma Inc., Japan
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007023775	A1	20070301	WO 2006-JP316349	20060822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2617519 A1 20070301 CA 2006-2617519 20060822
EP 1917979 A1 20080507 EP 2006-796612 20060822
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI JP 2005-241403 A 20050823
WO 2006-JP316349 W 20060822

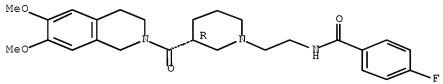
AB Disclosed is a therapeutic agent for atrial fibrillation comprising an If current inhibitor, particularly (-)-N-[2-[(R)-3-(6,7-dimethoxy-1,2,3,4-tetrahydro- isoquinoline-2-carbonyl)piperidino]ethyl]-4-fluorobenzamide monophosphate, as an active ingredient. This active ingredient has more preferred properties for use as a therapeutic agent for atrial fibrillation compared to verapamil (a Ca antagonist) and atenolol (a β-blocker) which have been conventionally used as the therapeutic agents for atrial fibrillation.

IT 312752-85-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for atrial fibrillation containing If current inhibitors)

RN 312752-85-5 CAPLUS

CN Benzamide, N-[2-[(3R)-3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:872791 CAPLUS Full-text

DN 141:350046

TI Preparation of novel crystal of fluorobenzamide derivative

IN Yoshida, Shinya; Watanabe, Toshihiro; Marumo, Kiyotaka; Yamaguchi, Sou

PA Yamanouchi Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

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PI	WO 2004089933	A1	20041021	WO 2004-JP4794	20040401
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SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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	EP 1609788	A1	20051228	EP 2004-725182	20040401
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	IN 2005DN04378	A	20070105	IN 2005-DN4378	20050927
	MX 2005PA10603	A	20060725	MX 2005-PA10603	20050930
	US 20070129357	A1	20070607	US 2005-552019	20051003
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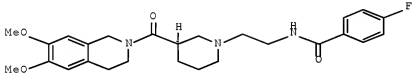


I

AB A novel crystal of (R)-(-)-N-[2-[3-[(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)carbonyl]piperidino]ethyl]-4-fluorobenzamide (I) monophosphate, which is known as a preventive and/or remedy for ischemic diseases such as angina pectoris and myocardial infarction and cardiovascular diseases such as ischemic heart failure and arrhythmia, was prepared and characterized by X-ray diffraction spectra and DSC. Two crystal forms (α and β crystal forms) of compound I were prepared α Crystal form of compound I exhibited excellent moisture adsorption property and is advantageous for handling and formulation. Thus, 206.4 g (R)-1-[2-[(4-fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid was treated with 810 mL DMF and 120.8 g 6,7-dimethoxy-1,2,3,4- tetrahydroisoquinoline monohydrochloride, stirred, cooled, treated with 53.22 g Et3N at ≤12°, treated with 217 mL DMF and then successively with 21.32 g 1H-1,2,3-benzotriazole and 121.0 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride at ≤5°, and stirred at 0-4° for 15.5 h, and treated with 340 mL H2O, 2,000 mL EtOAc, and 550 mL 8% (W/V) aqueous NaOH solution to give, after workup and concentration, crude free base I (83.9% purity). I (11.90 g) was dissolved in ethanol to a total weight of 97.8 g, treated with 5 mL ethanol, 0.47 g H2O, and 0.86 g 85% H3PO4, and then with 5 mL ethanol, stirred at 30° overnight, and filtered to give, after washing the crystals with ethanol and drying, 3.38 g I monophosphate (α crystal form).

IT 312752-86-6P, (R)-(-)-N-[2-[3-[(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)carbonyl]piperidino]ethyl]-4-fluorobenzamide monophosphate
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel crystal of fluorobenzamide monophosphate derivative having excellent moisture adsorption property)

RN 312752-86-6 CAPLUS

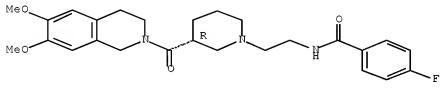
CN Benzamide, N-[2-[(3R)-3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-

isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro-, phosphate (1:1)
(CA INDEX NAME)

CM 1

CRN 312752-85-5
CMF C26 H32 F N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:565208 CAPLUS Full-text
DN 141:106387
TI Isoquinoline derivatives containing benzamide moiety and process for their preparation
IN Yoshida, Shinya; Watanabe, Toshihiro; Marumo, Kiyotaka; Kakefuda, Akio
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058710	A1	20040715	WO 2003-JP16582	20031224
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	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				

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	AU 2003292757	A1	20040722	AU 2003-292757	20031224
	CN 1753870	A	20060329	CN 2003-80109919	20031224
	IN 2005DN02787	A	20070105	IN 2005-DN2787	20050623
	US 20060084807	A1	20060420	US 2005-540421	20050624
	KR 758522	B1	20070914	KR 2005-711965	20050624
PRAI	JP 2002-375153	A	20021225		
	WO 2003-JP16582	W	20031224		

OS MARPAT 141:106387

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

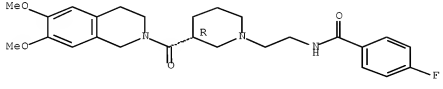
AB Process for the preparation of compds. I [R3 =, R4 = H, alkyl, alkoxy; Ar = (un)substituted aryl] and compds. II [R1 = H, alkyl, benzyl; R2 = H, protecting group of amino; Ar = (un)substituted aryl] were provided. For example, a mixture of compound (R)-II [R1 = Ethyl; R2 = H; Ar = 4-fluorophenyl] (37.94 g), e.g., prepared from (R)-piperidine-3-carboxylic acid Et ester L-tartaric acid salt in 4 steps, and 1 M aqueous NaOH (177 mL) in EtOH (100 mL) stirred at room temperature for 1 h. After treating the reaction with HCl to acidic pH, the solvent was azeotropically removed by toluene. Then, to a solution of the resulting residue in DMF (250 mL) were added 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (21.66 g), HOBt (7.97 g) and WSC hydrochloride (27.14 g) at 10 °C. The reaction was stirred at room temperature for 3 h, aqueous work-up followed by treatment with 85% phosphoric acid (13.65 g) in EtOH (500 mL) afforded claimed compound III phosphoric acid salt (44.25 g). Of note, compds. I are useful for prophylaxis and/or treatment of myocardial infarction, congestive heart failure, etc. (no data). The disclosed process employs less hazardous solvent.

IT 312752-85-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoquinoline derivs. via N-fluorobenzoylation of tetrahydroisoquinoline derivs.)

RN 312752-85-5 CAPLUS

CN Benzamide, N-[2-[(3R)-3-[(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)carbonyl]-1-piperidinyl]ethyl]-4-fluoro- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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